Adverse Reaction Workup Categories and Testing Protocols
Job Aid for the Transfusion Medicine Laboratory (TML)

Pre-transfusion Testing Categories for Saskatchewan Facilities	
Transfuse Only Facility	• No red blood cells held on site • No pre-transfusion testing performed on site • Transfuses crossmatched blood supplied by other facility
Hold/Transfuse Laboratory	• Holds O negative, Kell negative uncrossmatched red blood cells for transfusion in emergent situations • No pre-transfusion testing performed on site • Transfuses crossmatched blood supplied by other facility
Basic Testing TM Laboratory	• Basic pre-transfusion testing includes: Direct Antiglobulin Test, Group and Screen and crossmatching when no significant antibodies are detected
Advanced Testing TM Laboratory	• Pre-transfusion testing included: All testing performed at the Basic Testing laboratories, as well as basic antibody identification, antigen typing and crossmatching • Advanced Testing laboratories require at least two commercial manufactured antibody panels to complete basic antibody identification
Complex Testing TM Laboratory	• Full range of pre- and post-transfusion testing provided • Performs complex testing to determine basic and complex antibody identification • Complex testing laboratories require multiple commercially manufactured antibody panels and anti-sera to identify and exclude antibodies

CATEGORY OF WORKUP	CONDITION(S)	PROTOCOL

LEVEL 1 SEROLOGICAL INVESTIGATION	• If an adverse reaction is reported to the Transfusion Medicine Laboratory (TML)	• Request ward to send the following to the TML:
		  ○ patient's post-transfusion sample (2 EDTA vials)
		  ○ component bag or product container with the administration set/fluid
		  ○ component or product transfusion label/tag
		• **Complete Level 1 Serological Investigation as follows:**
		  ○ Lab clerical check of the:
		  ▪ component bag or product container
		  ▪ component or product transfusion label/tag
		  ▪ patient's pre- and post-transfusion samples
		  ▪ relevant records
		  ○ Visual plasma check on post-transfusion EDTA sample for hemolysis (slightly red to dark red or hemolyzed) or bilirubin (icteric, green, brown)
		  ○ Polyspecific DAT on the post-transfusion sample
		  ○ ABO/Rh on the post-transfusion sample
		• *If the transfusing facility is unable to perform any of the above testing, send required samples to the crossmatching facility*

	• If the results of the clerical check are incorrect or not identical	• Collect a new post-transfusion sample to confirm discrepant results • Search current files to determine if another patient is at risk
	• If the visual plasma check is positive	• Collect a new post-transfusion sample and repeat visual inspection of plasma • Visually inspect the donor unit(s) and segments for hemolysis, clots, purple color, etc. (refer to CBS Visual Inspection Tool available at https://professionaleducation.blood.ca/en/visual-inspection-tool) • Immediately contact the Transfusion Medicine Physician (TMP) on-call if there is evidence of a

		hemolytic transfusion reaction
		• A hemolysis work-up should be requested, including:
		  ○ Urinalysis on post-transfusion first voided urine
		  ○ CBC, direct and total bilirubin, reticulocyte count, haptoglobin, peripheral blood smear, urea, creatinine, electrolytes
		  ○ Consideration should be given to PTT, INR and fibrinogen testing

	• If the post-transfusion DAT result is positive	• Complete a polyspecific DAT on the pre-transfusion sample
		  ○ If the pre-transfusion DAT result is negative or at a weaker strength than the post-transfusion DAT result:
		  ▪ Review the patient's transfusion history and medication record to see if possible passive antibodies were acquired from transfusion or medications
		  ▪ Contact the TMP on-call if transfusion history or medication record indicates possible passive antibody
		  ▪ Perform Level 2 Serological Investigations or send the pre- and post-transfusion samples to a complex site for Level 2 Serological Investigations
		  ○ If the pre-transfusion DAT result is positive at the same strength or greater than the post-transfusion DAT result, no further investigation is required

LEVEL 2 SEROLOCIAL INVESTIGATION	• If any of the results of the Level 1 Serological Investigation are positive or abnormal	• Contact the TMP on-call to inform them of the need for a Level 2 Serological Investigation and verbally report and review the results of Level 1 testing
		• **Complete Level 2 Serological Investigation as follows:**
		  ○ ABO/Rh on pre-transfusion sample and implicated donor unit(s)
		  ○ Antibody screen (and identification if appropriate) on pre- and post-transfusion patient samples
		  ○ Perform an eluate if post-transfusion DAT is positive in recently transfused patient
		  ○ IAT crossmatch of implicated donor unit(s) using pre- and post-transfusion samples

	• If a discrepancy in ABO/Rh testing is identified between the pre- and post- transfusion patient samples or between ABO/Rh of donor unit and patient sample	• Stop all ongoing RBC transfusions and hold all pending RBC transfusions until it is confirmed that another patient is not at risk due to sample mix-up ("wrong blood in tube")
		• Inform the following individuals and/or facilities immediately:
		  ○ TMP on-call
		  ○ Local safety/risk management program
		  ○ Health Canada

	• If ABO discrepancy is identified between the ABO/Rh testing performed in local TML and the label on the donor unit provided by CBS	• Report to TMP immediately • Inform Canadian Blood Services immediately as this may impact companion products at collection facility

	• If IAT crossmatch identifies an incompatibility between the donor units and post-transfusion sample	• Report to the TMP on-call immediately
		• Further investigations to identify the cause of incompatibility must take place (refer pre- and post-transfusion samples to a complex site if the local site is not able to perform relevant investigations)
		• A hemolysis work-up should be requested from the health care team, including:
		  ○ Urinalysis on post-transfusion first voided urine
		  ○ CBC, direct and total bilirubin, reticulocyte count, haptoglobin, peripheral blood smear,

		urea, creatinine, electrolytes ○ Consideration should be given to a PTT, INR and fibrinogen testing
	• If antibody screen on the post-transfusion sample is positive, suggestive of a new antibody	• Perform antibody identification on pre- and post-transfusion samples • Crossmatch available segments of any units transfused within the previous 3 months with pre- and post-transfusion samples • The pre- and post-transfusion segments and available red cell unit segments must be referred to the complex site if local site cannot perform the relevant investigations
BACTERIAL CONTAMINATION OR SEPSIS	• If the component/product appears to be contaminated with bacteria in visual inspection; or • If the patient has any ONE of the following signs or symptoms ○ Temp rise ≥ 39°C **OR** ○ Temp rise ≥ 2°C from pre-transfusion baseline and/or any of the following symptoms: ▪ Hypotension ▪ Tachycardia ▪ Shock ▪ Dyspnea ▪ Shaking chills ▪ Rigors	• Perform aerobic and anaerobic blood cultures and gram stain on returned blood component (NOT the segment) or blood product • Collect aerobic and anaerobic blood cultures on patient (taken from different sites) • Report to CBS or Product Manufacturer and Health Canada as soon as bacterial contamination is suspected, based on component or product appearance, patient clinical condition, or preliminary bacterial culture results.
TRALI	• If the patient's condition meets the following definition of Acute Lung Injury (ALI): ○ Acute onset (during or within 6 hours after completion of transfusion) ○ Hypoxemia ▪ PaO_2 / FiO_2 < 300 **OR** ▪ Oxygen saturation is < 90% on room air **OR** ▪ Other clinical evidence ○ Bilateral lung infiltrates on frontal chest X-ray ○ No evidence of circulatory overload (diuretics ineffective) • TRALI can occur in patients with no pre-existing respiratory symptoms (confirmed TRALI) or in those with pre-existing system/respiratory disorders (possible TRALI)	• Contact the TMP on-call • To report a TRALI or possible TRALI to Canadian Blood Services (CBS): ○ Contact CBS directly to initiate reporting. ○ Submit a completed a completed TRALI Patient Data Form to CBS. The required form can be retrieved from https://professionaleducation.blood.ca/sites/default/files/trali_patient_data_form_2020-11-12_1.pdf ○ Submit patient TRALI samples to the Winnipeg National Platelet Immunology Reference Laboratory (NPIRL) accompanied by a completed requisition for donor HLA and HNA antibody testing ▪ Information on sample submission can be retrieved from https://www.blood.ca/en/laboratoryservices/trali-investigation ▪ The required requisition can be retrieved from https://www.blood.ca/en/laboratory-services/trali-investigation • To report a TRALI or possible TRALI to Health Canada's Canada Vigilance Program, fax completed de-identified SK TAER Form to 1-866-678-6789

SEVERE ALLERGIC OR ANAPHYLACTIC REACTION	• If the patient experiences the following in addition to allergic mucocutaneous symptoms:
	  ○ Hypotension and/or respiratory compromise (e.g. bronchospasm, angioedema, stridor, hypoxia) requiring urgent cardiorespiratory support
	  ○ Altered consciousness or circulatory collapse
		• Contact the TMP on-call
		• Perform Level 2 Serological Investigations if indicated by TMP:
		  ○ Serum Haptoglobin level
		  ○ Serum IgA level
		  ▪ If the serum IgA is <0.06 g/L, consideration will be given to anti-IgA testing
		  ○ Referral of the pre-transfusion EDTA sample to the CBS National Immunohematology Reference Laboratory (NIRL), Brampton, Ontario for further testing to rule out an anti-Chido or anti-Rogers, if a non-specific antibody is detected on antibody screen
		• Immediately report to CBS or Product Manufacturer and Health Canada